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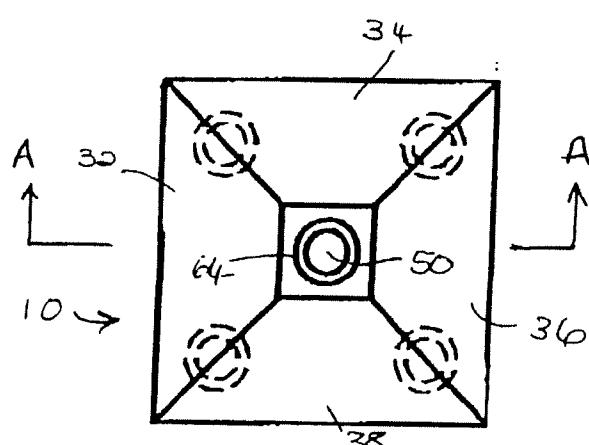
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(54) Title: SPOT MARKER FOR USE IN IMAGING PROCEDURES



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(57) Abstract: A spot marker (10) for use in an imaging procedure contains an amount of a detectable substance (50) which generates its own image in the imaging procedure. In one embodiment, two or more different detectable substances are used (50, 64), allowing the spot marker to be used in multi-modality fusion imaging- the combination of images from two or more different imaging procedures, such as CT, PET, SPECT, and MRI, to produce a combination image. In another embodiment, the marker (10) is configured for enabling three dimensional alignment of images from one or more different imaging procedures.

SPOT MARKER FOR USE IN IMAGING PROCEDURES

Background of the Invention

The present invention relates to the field of radioisotope studies. It finds particular application in conjunction with radioactive sources for Positron Emission Tomography (PET) applications and for multi-modality 5 imaging, and will be described with particular reference thereto. It should be appreciated, however, that the invention is also applicable to other imaging systems.

In nuclear medicine, images of internal structures or functions of the body are acquired by using gamma cameras 10 (or "Anger cameras") to detect radiation emitted by a radio-pharmaceutical that has been injected into the patient's body. A computer system controls the gamma camera to acquire data and then processes the acquired data to generate the images. Nuclear medicine imaging techniques 15 include single-photon emission computed tomography (SPECT) and positron emission tomography (PET). SPECT imaging is based on the detection of individual gamma rays emitted from the body, while PET imaging is based on the detection of gamma ray pairs emitted in coincidence in opposite 20 directions due to electron-positron annihilations. Accordingly, PET imaging is sometimes referred to as coincidence imaging.

Gamma radiation is produced by the nuclei of certain radioactive atoms during annihilation of positrons by 25 electrons. When most radioactive isotopes decay, they emit single gamma rays of very specific energy, measured in keV. For example, the primary gamma ray of Co-57 is 122 keV and for Tc-99, it is 140 keV. Because different energy levels give different performance characteristics for imaging, a

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prime consideration for the choice of isotope in nuclear medicine is the energy level of the isotope. Gamma-ray or scintillation cameras monitor the progress or distribution of a gamma-ray emitting nuclide introduced into a patient.

5 The camera is located adjacent the part or organ of the patient concerned, for instance the brain or liver, and the distribution of the nuclide therein is indicated by the activity at various positions within the organ recorded by the camera. Gamma cameras, used in SPECT nuclear medicine,

10 are designed to allow the detection of a single photon energy level (keV) emitting from isotopes. Such cameras require the use of special filters, called collimators, to detect where the photon originated. The filters, however, result in the loss of a very high percentage of the useful

15 information.

Positron emitting isotopes used in PET imaging differ from other radioactive isotopes in that positrons (positive electrons) are emitted from proton-excess radioactive nuclides. The emitted positrons almost instantly collide

20 with a negative electron. This encounter results in the annihilation of both particles, with the creation of two gamma rays of exactly 511 keV, the energy equivalent of two electron masses. These annihilation photons travel in 180 degree opposite directions. Thus, all positron-emitting

25 isotopes have exactly the same energy for imaging.

Positron Emission Tomography (PET) cameras are becoming increasingly used in nuclear medicine for a variety of applications. They are particularly useful in the field of oncology, for the study of breast cancer and other cancers.

30 A PET camera is similar in some respects to a Gamma camera. A typical PET camera consists of a polygonal or circular ring of radiation detection sensors placed around a patient area. Radiation detection begins by injecting isotopes with short half-lives (e.g., F-18 Fluorodeoxyglucose (FDG)) into

35 a patient's body, which is then placed within a patient area. The isotopes are absorbed by target areas within the body causing the isotope to emit positrons that are detected

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when they generate gamma rays. When in the human body, the positrons collide with electrons and the two annihilate each other, releasing gamma rays. The emitted rays move in opposite directions, leave the body and strike the ring of 5 radiation detectors.

PET cameras differ from conventional Gamma cameras in that they do not require collimators for point of origin determination. Instead, they use what is known as coincidence detection. The ring of detectors includes an 10 inner ring of scintillator crystals and an outer ring of light detectors or photomultiplier tubes. The scintillator crystals respond to the incidence of gamma rays by emitting a flash of photon energy (scintillation) that is then converted into electronic signals by a corresponding 15 adjacent photomultiplier tube. PET scanners detect whether two photons hit the detectors simultaneously, or in coincidence. If two such photons are detected, then knowing that the photons arrived from the same atom at 180 degree opposite angle, the camera's computer can plot where the 20 atom was located by drawing a line between the two points of incidence. If only a single photon is detected, however, the photon is rejected as scatter. Thus, single photon-emitting isotopes do not show up on a PET scanner.

In many cases, the same gamma cameras are used to 25 perform SPECT and PET studies. Different electronics are provided for each type of study.

Spot markers are used as positioning aids in SPECT and other types of imaging. A small marker containing a radioactive isotope or other detectable substance, is placed 30 on a particular spot on a patient. It might mark the navel, Adam's apple, etc. When the study is repeated in the future, the marker can be placed in the same position on the body and the two scans can then be lined up exactly. The spot marker can also be used as a reference. For example, 35 in determining the distance of a tumor from the patient's Adam's apple. Currently, there are no spot markers available for PET imaging.

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Recently, a technique known as "fusion imaging" has been used to generate images of a patient's body, as disclosed, for example in U.S. Patent No. 5,799,099 to Wang, et al. This technique combines the scans from two different 5 types of imaging techniques, such as x-ray computer tomography (CT) with magnetic resonance imaging (MRI), to provide more comprehensive information. Bone, for example, is seen best on CT images, while soft-tissue structures are best seen by magnetic resonance imaging MRI. Because of the 10 complementary nature of the information in these two imaging modalities, the registration of MR images with CT images is of growing importance for diagnosis and for surgical planning. Furthermore, for the purpose of navigation during surgery it is helpful to be able to register images to the 15 patient anatomy itself. Registration is defined herein as the determination of a one-to-one mapping between the coordinates in one space and those of another, such that points in the two spaces that correspond to the same anatomic point are mapped to each other.

20 However, problems arise when the scans are attempted to be aligned, since there are currently no spot markers which show up in two forms of scan.

25 X-ray computer axial tomography (CAT) scanners utilize a rotating gantry to obtain multiple X-ray images, or "views", at progressively different rotational angles. Each 30 set of images is referred to as a "slice". A patient is disposed in a central opening of the gantry on a table which is movable axially, thereby enabling slices to be obtained at multiple axial positions as well. All of the slices obtained are then processed in a computer according to known 35 algorithms to produce enhanced images for diagnostic purposes.

In MRI scanners, the patient's body is placed within a subject receiving space of a primary field magnet and 35 exposed to a strong, substantially constant, primary magnetic field. The atomic nuclei spin around axes aligned with the magnetic field. Powerful radio frequency "RF"

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signals are broadcast into the subject receiving space to excite atomic nuclei within the patient's body into a resonance state in which the spinning nuclei generate minuscule RF signals, referred to herein as magnetic 5 resonance signals. By applying magnetic field gradients so that the magnitude of the magnetic field varies with location inside the subject-receiving space characteristics of the magnetic resonance signals from different locations within the region, such as the frequency and phase of the 10 signals, can be made to vary in a predictable manner depending upon position within the region. Thus, the magnetic resonance signals are "spatially encoded" so that it is possible to distinguish between signals from different parts of the region. After repeating this procedure with 15 various different gradients, it is possible to derive a map showing the intensity or other characteristics of the magnetic resonance signals versus position within the excited region. Because these characteristics vary with concentration of different chemical substances and other 20 characteristics of the tissue within the subject's body, different tissues provide different magnetic resonance signal characteristics which can be used to generate a visible picture of structures within the patient's body.

The present invention provides a new and improved spot 25 marker which overcomes the above-referenced problems and others.

Summary of the Invention

In one embodiment of the present invention, a multi-modality spot marker for use as a positioning aid in imaging 30 procedures is provided. The spot marker includes a body and a plurality of detectable substances supported by the body in fixed relation to each other. A first of the detectable substances is detectable in a first of the imaging procedures and a second of the detectable substances is 35 detectable in a second of the imaging procedures, but not in the first of the imaging procedures.

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In accordance with another aspect of the present invention, a spot marker for use as a positioning aid in an imaging procedure is provided. The spot marker includes a body. At least one detectable substance, which is 5 detectable in the imaging procedure, is supported by the body. The detectable substance defines four points in fixed relation to each other, allowing alignment in three dimensions of an image produced by the imaging procedure in which the at least one detectable substance is detectable.

10 In accordance with another aspect of the present invention, a method of multi-modality imaging is provided. The method includes positioning a spot marker in fixed relation to a subject which is to undergo imaging. The method further includes subjecting the subject to first and 15 second imaging procedures to produce first and second images of the subject. The first imaging procedure generates an image of a first detectable substance carried by the spot marker on the image of the subject. The second imaging procedure generates an image of a second detectable substance carried by the spot marker on the second image of the subject, but not an image of the first detectable substance. The images are aligned using the images of the 20 first and second detectable substances.

25 In accordance with another aspect of the present invention, a method of imaging is provided. The method includes positioning a spot marker in fixed relation to a portion of a subject to undergo imaging. The spot marker includes amounts of a detectable substance which define four spaced points in three dimensions. A first image of the 30 subject is produced using a first imaging procedure. The first imaging procedure generates images of the four spaced points defined by the amounts of detectable substance. A second image of the subject is produced using a second imaging procedure. The second imaging procedure generates 35 images of the four spaced points defined by the amounts of detectable substance. The first and second images are

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aligned using the positions of the four spaced points on the first and second images.

In accordance with another aspect of the present invention, a method of forming a spot marker for use in two different imaging procedures is provided. The method includes supporting an amount of a first detectable substance on a support body. The first detectable substance includes a radionuclide which is detectable in a first imaging procedure. An amount of a second detectable substance, which is different from the first detectable substance, is supported on the support body in a fixed position relative to the amount of the first detectable substance. The second detectable substance is detectable in a second imaging procedure.

One advantage of at least one embodiment of the present invention is the provision of a spot marker for PET imaging studies.

Another advantage of at least one embodiment of the present invention is that it enables multi-modality images to be aligned.

Another advantage of at least one embodiment of the present invention is that it allows alignment of images in three dimensions.

Still further advantages of the present invention will become apparent to those of ordinary skill in the art upon reading and understanding the following detailed description of the preferred embodiments.

Brief Description of the Drawings

The invention may take form in various components and arrangements of components, and in various steps and arrangements of steps. The drawings are only for purposes of illustrating a preferred embodiment and are not to be construed as limiting the invention.

FIGURE 1 is a side sectional view of a first embodiment of a spot marker according to the present invention;

FIGURE 2 is a top view of the spot marker of FIGURE 1;

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FIGURE 3 is a bottom view of the spot marker of FIGURE 1;

FIGURE 4 is a perspective view of the spot marker of FIGURE 1;

5 FIGURE 5 is an enlarged side sectional view of the top of the spot marker of FIGURE 1;

FIGURE 6 is a side sectional view of a second embodiment of a spot marker according to the present invention;

10 FIGURE 7 is a top view of the spot marker of FIGURE 6;
FIGURE 8 is a bottom view of the spot marker of FIGURE 6;

FIGURE 9 is a schematic view of a third embodiment of a spot marker according to the present invention;

15 FIGURE 10 is a schematic view of a fourth embodiment of a spot marker according to the present invention;

FIGURE 11 is an enlarged side sectional view of the top of a fifth embodiment of a spot marker according to the present invention;

20 FIGURE 12 is a perspective view of a sixth embodiment of a spot marker according to the present invention;

FIGURE 13 is a perspective view of a seventh embodiment of a spot marker according to the present invention;

25 FIGURE 14 is a side sectional view of an eighth embodiment of a spot marker formed in a mold according to the present invention;

FIGURE 15 is a top view of the spot marker of FIGURE 14;

30 FIGURE 16 is a side sectional view of a ninth embodiment of a spot marker in accordance with the present invention; and

FIGURE 17 is a perspective elevational view of the spot marker of FIGURE 1 on a patient in a combined SPECT/PET imaging system according to the present invention.

35 Detailed Description of the Preferred Embodiments

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With reference to **FIGURE 1**, a spot marker 10 for use in an imaging procedure is shown. The term "imaging procedure," as used herein, means a procedure in which a subject, such as a human body or part of the body is

5 examined by exposing the body to an image generating source, which may be a source of radiation, such as x-rays or gamma rays, or a magnetic source, and a detection device, from which features of the body can be identified. Such procedures include, but are not limited to Positron Emission

10 Tomography (PET), Single Photon Emission Tomography (SPECT), Computerized Tomography (CT), also known as Computerized Axial Tomography (CAT), and Magnetic Resonance Imaging (MRI). The device for performing the particular procedure is referred to generally herein as a scanner.

15 In Positron Emission Tomography (PET) scanners the source of radiation includes an isotope with short half-life (e.g., F-18 Fluorodeoxyglucose (FDG)) which is injected into a patient's body. The isotope is absorbed by target areas within the body causing the isotope to emit positrons that

20 are detected when they generate gamma rays. When in the human body, the positrons collide with electrons and the two annihilate each other, releasing gamma rays. The emitted rays move in opposite directions, leave the body and strike the ring of radiation detectors. The PET detector detects

25 gamma ray pairs emitted in coincidence in opposite directions due to electron-positron annihilations.

SPECT imaging is based on a similar procedure, but the detection is of individual gamma rays emitted from the body. SPECT imaging typically uses a gamma scintillation camera

30 (GSC), with a so-called "position sensitive" continuous-area detector and a single photon gamma emitter. Such cameras allow planar static and dynamic studies as well as SPECT studies. Scanners which allow both SPECT and PET imaging may also be used.

35 Computerized Axial Tomography (CAT) scanners typically employ a source of x-rays, positioned adjacent the patient's body, and a rotating gantry to obtain multiple X-ray images,

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or "views," at progressively different rotational angles. Each set of images is referred to in the art as a "slice".

In MRI scanners, the patient's body is exposed to a strong, substantially constant primary magnetic field.

5 Powerful radio frequency "RF" signals are broadcast to excite atomic nuclei within the patient's body into a resonance state in which the spinning nuclei generate minuscule RF signals, referred to herein as magnetic resonance signals.

10 The spot marker 10 is used as a positioning aid in imaging and may be placed, for example on a recognizable spot on the patient's skin 12, such as on the navel or Adam's apple. Adhesive tape 14, or other suitable positioning member, may be used to hold the marker 10 in 15 place during an imaging procedure. Additionally, or alternatively, a line can be drawn around the marker 10 on the patient's skin so that it can be repositioned on the skin at a later time or in a subsequent imaging procedure.

20 In preferred embodiments of the present invention, the spot marker 10 allows three dimensional alignment of images ('registration') from a first imaging procedure and a second imaging procedure. The first and second imaging procedures may be undertaken with the same type of scanner or with different types of scanner. For example, the first and 25 second imaging procedures may both be PET scan, taken at different times. This allows a physician to review changes that have occurred in the patient's body in the intervening period. Or, the two imaging procedures may be different, to allow a fusion image to be created. By fusion image it is 30 meant a combination image from two or more different types of scan. This allows, for example, images from the following combinations to be achieved: PET/CT; PET/SPECT; PET/MRI; SPECT/CT; SPECT/MRI; MRI/CT; PER/SPECT/CT; and so forth. The two different procedures may be performed by the 35 same scanner, such as a scanner capable of performing both PET and SPECT scans, or may be performed by different scanners.

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To allow a three dimensional alignment (registration) of two images, it is desirable to be able to align the images in three axial directions. One way to do this is to define two of the dimensions by a plane with three (or more) 5 fixed points and to define the third dimension in a second plane spaced from the first plane, for example by a fourth (or more) fixed point. This allows alignment of the image in three dimensions.

The spot marker 10 preferably is constructed so as to 10 maintain the positions of the four (or more) fixed points fixed in relation to one another. By way of example, the spot marker 10 of **FIGURES 1-5** defines the four fixed points in a generally pyramidal body 20. The spot marker 22 of **FIGURES 6-8** uses a cube-shaped body 24 to define the four 15 fixed points. The size of the body 20, 24 is not critical, although a body having each of its sides about 2-3 cm in length is suitable for most imaging procedures.

The pyramidal spot marker 10 shown in **FIGURES 1-5** has a square base 30 and four generally triangular sides 32, 34, 20 36, 38. The edges of the pyramid may be rounded slightly to avoid having sharp edges or corners. Four fixed points P_1 , P_2 , P_3 , P_4 are spaced from each other in the same plane, substantially parallel with, and closely adjacent to the base 30 (**FIG. 4**). To maximize the spacing, the points are 25 preferably adjacent the corners. A fifth fixed point P_5 is defined adjacent the top of the pyramid and vertically spaced from the points P_1 , P_2 , P_3 , P_4 . The fixed points P_1 , P_2 , P_3 , P_4 may each be centered, for example on one of the two axes of the base x , y , as shown in **FIGURE 3**, with the fifth 30 fixed point P_5 at the intersection of the two axes, as viewed from above. It will be appreciated that since only three points are needed to define the plane, one of the four points P_1 , P_2 , P_3 , P_4 may be eliminated. For example, a pyramid with a triangular base could be used with three 35 points P_1 , P_2 , P_3 spaced from each other adjacent corners of the triangular base, and a fourth point in the same location as P_5 .

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In the cube-shaped spot marker 22 of FIGURES 6-8, the fixed points P_6 , P_7 , P_8 , P_9 and P_{10} are positioned in generally the same locations as the fixed points P_1 , P_2 , P_3 , P_4 , P_5 , with the point P_{10} adjacent the center of the top of 5 the cube and the points P_1 , P_2 , P_3 , P_4 adjacent the bottom of the cube.

Each of the fixed points is defined by at least one detectable substance. Specifically, the spot marker 10, 22 contains a small amount of at least one and preferably two 10 or more detectable substances. The detectable substance is one which is detectable in an imaging procedure, such as those described above. For comparing images from two different procedures, two detectable substances are preferably employed, namely a first detectable substance 15 which is detectable in a first imaging procedure and a second detectable substance which is detectable in a second imaging procedure, although if a detectable substance is used which can be detected by both imaging procedures, then only one detectable substance need be used.

Having two (or more) detectable substances which are detectable by different detectors allows the same spot marker 10, 22 to be used in two (or more) different types of imaging procedures. The spot marker can be positioned on the patient's body and left in place throughout both imaging 25 procedures. Additionally, the spot marker may be used for fusion imaging-the combination of images from two or more different types of imaging procedures. As will be described in greater detail below, the spot marker enables the two images to be superimposed and details from both images to 30 become visible on a single combination image. The image may be two dimensional or three dimensional. Additionally, while the fixed points are described as being spaced from one another, it is to be appreciated that the term "spaced" is used to cover embodiments in which the fixed points are 35 joined, as by a line or plane of detectable material.

In a first embodiment, the spot marker contains a small amount of a radionuclide which is detectable in a

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radiological scanning procedure. For PET imaging, the marker includes a positron-emitting isotope or isotopes, such as Na-22 or Ge-68/Ga-68. For SPECT imaging, a radioisotope such as Co-57 may be used.

5 The positron-emitting isotope or other radioactive source is present in sufficient quantity to act as a spot marker for a radiation camera, such as a PET camera system, without posing a significant risk of radiation damage to the patient. For example, in the case of Na-22, the spot marker
10 10, 22 may have from about 1-200 μ Ci of activity, more preferably, up to about 12 μ Ci of activity, and most preferably, about 10 μ Ci of activity.

Other detectable substances may be used for other imaging procedures. For MRI scanning, a material with a
15 high proton content is preferred. For example, an oil or wax, such as a lump of a water insoluble wax, such as beeswax, or a piece of an almond may be used for MRI scanning. For CT scanning a material with a relatively high density, relative to body tissue, is preferred, such as
20 stainless steel or aluminum, which may be in the form of a small pellet.

In the embodiment of **FIGURES 1-5**, for example, a small pellet 50 of radioactive material or other detectable substance is positioned in a recess or cavity 56, extending
25 in to the pyramid in the vicinity of the fixed points, as best shown in **FIGURE 5**. The cavity may be, for example, a tubular or square bore of about 0.5-1 cm in diameter. Or, as shown in **FIGURE 1**, may have portions 58, 60 of different diameters for separately accommodating two or more
30 detectable substances. The pellet 50 may be press fit into the cavity 56 or held in place by a retaining member, such as an adhesive material or cap (not shown). Or, the pellet may be formed by introducing the radioactive substance in liquid form, e.g., in a binder and allowing the
35 binder/radioactive material to harden. Where two detectable substances are used, the second detectable substance may be placed in the same cavity. For example, as shown in **FIGURE**

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5, a block 64 of a second detectable substance is positioned in the cavity above the pellet of the first detectable substance. As shown in **FIGURE 3** the lowermost piece of detectable substance 50, as viewed from above, may be larger
5 than the first piece of detectable substance 64, so that the first detectable substance 50 extends beyond the edges of the second detectable substance 64, and thus is readily detected from above by the scanner detector. Or, where the one of the scanners is capable of detecting a detectable
10 substance 50 which is covered by the other substance 64, the substance 50 may be underneath, and completely covered by the other substance 64, as viewed from directly above (**FIGURE 5**). For example, in the embodiment of **FIGURE 5**, a radioactive material 50 for use in PET or SPECT scanning is
15 below a block 64 of beeswax for MRI scanning or a pellet 64 of steel or aluminum for CT scanning. Suitable sized pellets for this purpose are BB gun pellets. Certain configurations of the body may be more preferable, depending on the nature of the detectable materials to be used. For
20 example, it may be easier to introduce a relatively large block of beeswax into a cube-shaped body 24 than into a pyramidal body 20.

In an alternative embodiment shown in **FIGURE 9**, the two detectable substances 50, 64 are placed in separate
25 cavities, which are spaced from each other, as viewed from above. Or, as shown in **FIGURE 10**, each of three or four base cavities 70, 72, 74, 76 contains at least one of the two detectable substances and the top cavity 78 contains both detectable substances.

30 In the embodiment of **FIGURE 11**, one of the detectable substances in the spot marker 10 is in the form of a coil 80 or a tube or otherwise surrounds the other detectable substance 82.

In the embodiment of **FIGURE 12**, a spot marker 83 has a
35 body 84 is in the form of a thin block 85, such as a disk, with cavities 86 (three are shown) containing amounts 88 of one or more detectable substances for defining the plane.

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The body 84 also includes a post 90, extending generally vertically from about the midpoint of the block 85, the fourth fixed point being defined by the post itself or by an amount 88 of the detectable substance within a cavity 92 at 5 or adjacent the top of the post.

The body 20, 24, 84 is preferably formed from a relatively rigid material, which maintains its shape during the scanning procedures and over time. The body is also preferably transparent to the scanning procedures in which 10 it is to be used. By "transparent" it is meant that the detectable substance can be detected through the body material. One suitable material for forming the body is Lucite, since it is transparent to many scanning procedures. It will be appreciated that although the body 20, 24 has 15 been described in terms of a solid, with cavities for the detectable substances, the body may be partially solid or formed simply as a frame, to which the detectable substances are affixed, either directly, or in a holder (see, e.g., FIG 12). If the body is formed as a frame, the body itself may 20 supply one of the detectable substances. For example the body may be formed as a frame comprising eight connected posts defining the shape of a square based pyramid. The posts may be formed, for example of aluminum or steel for CT scanning, with beeswax smeared over each of the posts, or at 25 the corners where the posts intersect, for MRI scanning.

The spot marker 10, 22 is preferably formed of sufficiently durable materials that it can be reused many times. After an imaging procedure, the tape is removed. If the spot marker contains a radioactive isotope, the spot 30 marker is preferably stored in a case designed for storage of radioactive materials.

The radioactive material for the spot marker 10, 22, 83 may be manufactured by mixing a known quantity of the selected positron-emitting isotope or other radioactive 35 material with a curable resin, such as a casting epoxy, e.g., a high impact epoxy resin, and dispensing the mixture directly into the cavities 56 of the body. The epoxy is then

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allowed to cure. Alternatively, the resin/radioactive material may be poured into a recess area in a mold and allowed to cure. The cured mixture is removed from the mold, or used still in the mold. For example chemically 5 bonding can be used to fix the cast material within the cavities 56. Solvent fuse sealing with dichloroethane or other suitable solvent, is one way of adhesively fixing the material in the cavity 56. Alternatively, a known quantity of the selected positron-emitting isotope or other 10 radioactive material is mixed with a solvent, such as water. The mixture is dispensed into the recess area of a mold and allowed to dry to a solid salt. The salt is then covered with casting epoxy, as described above, and the epoxy allowed to cure. The recess area is inserted and chemically 15 bonded into the body. Or, this procedure may be used to form the radioactive material in the body recess 56 directly.

The resin or mold container may be color coded according to the source material, for example, yellow for Na-22, black for Ge-68, red for Co-57. A source 20 identification label on the body 20, 24, 84 indicates the selected positron-emitting or other isotope, the production date, nominal activity, and the like.

While the spot marker 10, 22 has been described with reference to a three-dimensional structure for allowing the 25 registration of two scanning images, it will be appreciated, however, that a multi-modality spot marker can be formed with fewer than four fixed points. While such spot markers are less accurate at matching up images from two imaging procedures, they are less expensive to make and have utility 30 particularly when the position of the body feature under investigation does not need to be accurately located, either because of its size or location.

For example, a spot marker 100 may be formed with a body 110 having a single cavity 120, containing two 35 detectable substances 50, 64, as shown in **FIGURE 13**. In the embodiment of **FIGURE 13**, the body 110 is in the shape of a disk, with the cavity extending into the center of the disk

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from an upper surface 122 thereof, although other convenient shapes are also contemplated. The detectable substances 50, 64 may be any of those previously described. Or, two or three cavities may be used, e.g., one for each detectable 5 substance 50, 64, or an amount thereof.

As shown in **FIGURES 14** and **15** a spot marker 123 may contain only one fixed point and one detectable substance, such as a positron emitting isotope of the type described above (e.g. Na-22 or Ge/Ga-68) for PET imaging. In this 10 case, the body 124 may be in the form of a mold with a cavity 126. The radioactive isotope 128 is positioned generally at the center of the cavity and an epoxy material 130 poured into the cavity and allowed to harden to hold the radioactive isotope in place. Other methods for forming 15 spot markers may alternatively be used to form a PET marker of the present invention.

with reference to **FIGURE 16**, a spot marker 132 is formed with a body 133 which is preferably in the general shape of a disk, similar to that of **FIGURE 13**. A generally 20 cylindrical cavity 134 extends into the disk 134 from an upper surface 135 thereof. The cavity 134 contains two detectable substances 136, 138 as illustrated. Specifically, the first detectable substance 136 includes a radioisotope, which is combined with a resin, such as the 25 epoxy resin previously described. To form the spot marker 132, a portion 136A of the resin and isotope mixture is poured into the mold cavity 134. A pellet 139 of the second detectable substance 138 (such as a metal, oil containing substance, or wax) is then placed in the cavity on top of 30 the first layer 136A of the mixture, preferably before the resin has cured. A second portion 136B of the resin/isotope mixture is poured into the cavity 134, to form a second layer, covering the top of the pellet 139. In this way, the pellet 139 is surrounded by the resin/isotope mixture. A 35 detector positioned either adjacent the top surface 135 or bottom surface 140 of the mold 133 thus receives similar radiation levels from the marker 132, since the pellet 139

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is spaced from the detector by a layer of the isotope-containing mixture.

The use of the spot marker will now be described with respect to an exemplary dual modality imaging procedure, 5 although it will be appreciated that the marker may also be used in a single modality imaging procedure. For ease of reference, only the spot marker 10 is shown, although it will be appreciated that other spot markers described herein may alternatively be used. The spot marker 10 is attached to 10 the patient's skin 12, or other part of a subject 143 to be examined, and the patient is subjected to a first imaging procedure. The patient is then subjected to a second imaging procedure, with the spot marker located in the same position on the patient's skin 12. The correct positioning 15 for the second procedure may be achieved simply by leaving the spot marker in place and conducting the two procedures at the same time or consecutively. Or, the spot marker may be removed between the two imaging procedures and repositioned either by placing the marker in an outline 20 drawn around the spot marker before removal of the marker, or from measurements taken from the spot marker to an identifiable part of the body, such as the navel or Adam's apple. It will be appreciated that it is not necessary to use the same spot marker for each procedure. If a hospital 25 or other imaging facility keeps a number of nominally identical spot markers available, a second spot marker which is substantially identical in its configuration for purposes of identifying the fixed points may be substituted for the first spot marker in the second imaging procedure.

30 For example, one of the imaging procedures may include forming an image using a Positron Emission Tomography (PET) camera. With reference to FIGURE 17, a combination PET/SPECT camera system 144 suitable for use in both PET and SPECT imaging consists of a polygonal or circular ring 150 of 35 radiation detection sensors 152 placed around a patient receiving area 154. Radiation detection includes injecting isotopes with short half-lives into a patient's body

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placeable within the patient area 154. Suitable positron isotopes for PET scanning include Rb-82, F-18-deoxyglucose tracers (FDG), and thymidine. The isotopes are absorbed by target areas within the body causing the isotope to emit 5 positrons that are detected when they generate gamma rays. When in the human body, the positrons collide with electrons and the two annihilate each other, releasing gamma rays. The emitted rays move in opposite directions, leave the body and strike the ring 150 of radiation detectors 152. The 10 detectors also detect the detectable substance in the spot marker 10, and the fixed points of the spot marker show up on the images generated.

The ring 150 of detectors typically includes an inner ring of scintillator crystals and an outer ring of light 15 detectors or photomultiplier tubes (not shown). The scintillator crystals respond to the incidence of gamma rays by emitting a flash of photon energy (scintillation) that is then converted into electronic signals by a corresponding adjacent photomultiplier tube. A processing system 160 20 records the location of each energy flash and then plots the source of radiation within the patient's body by comparing flashes and looking for pairs of flashes that arise from the same positron-electron annihilation point. It then translates that data into a PET scan image. A PET monitor 25 162 preferably displays the concentration of isotopes in various colors indicating level of activity. By arranging the detector ring about the patient's body, location of each energy flash arising from the positron-electron annihilation can be recorded along a plane between the ring of detectors. 30 Thus, two-dimensional slice diagrams of the flash point can be produced indicating the area of interest. The resulting PET scan image indicates, for example, a transaxial view of neoplasms or tumors existing in the patient's body.

A spot marker 10, as described above, comprising a 35 positron-emitting isotope or isotopes as one of the detectable substance is used with the PET system described

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above and produces its own distinctive image on the image of the patient's body being generated.

The PET imaging procedure is followed by, preceded by, or carried out at the same time as a second imaging 5 procedure using a different type of scanner, such as a SPECT, CT, or MRI scanner. In the embodiment of **FIGURE 17**, for example, the present invention may be implemented in a dual-detector gamma camera system that is capable of both PET and SPECT imaging. The SPECT part of the system 10 includes detector heads 170, 172 mounted to a rotatable gantry (not shown). The detector heads include collimators situated in front of scintillation crystals. An array of photomultiplier tubes receive flashes of light generated when gamma rays strike the scintillation crystals. The 15 tubes send electrical signals to a processing system 176, which may be integrated with or separate from the processing system 160. The processing system 176 translates that data into a SPECT scan image.

The methods for operating CT and MRI scanners are well 20 known and will not be described in further detail here. For purposes of the invention, each of the imaging systems used to create a fusion image provides data to a processing system 180 from which an image of the patient's body is generated.

25 The processing system 180 is used to create a fusion image, in which the two images from the different procedures are superimposed, using the processing system and the portions of the images which are produced by the spot marker. The processing system 180 used for creating the 30 fusion image may be the same system as is used in producing the two separate images or may be a separate processing system which uses the two images, or is fed with data corresponding to the two images in order to create a fusion image.

35 By "alignment" it is meant that the two images to be "fused" are moved (or one of the images is moved), relative to one another, until the fixed points of the spot marker

come into alignment. If the images are taken from directly above or directly below the spot marker, the central spot generated by the detectable substances will be in the middle of the four base spots in both images. However, if the 5 images are taken at an angle relative to the top or bottom of the spot marker, the central spot will be offset accordingly. If the central spot is offset by the same amount in both images (i.e., the spot marker images can be superimposed, the images themselves are superimposable 10 (registration), i.e., have been taken through the same section of the body. Obviously, images which are not taken through exactly the same section of the body can be roughly superimposed, although losing some of their clarity and accuracy. The closer the spot marker images are in terms of 15 superimposability, however, the more accurate and clear the resulting fused image will be.

In an alternative embodiment, a first (e.g., PET) imaging procedure, in which the spot marker is used during production of a first image, is followed, at some time 20 thereafter, by a second imaging procedure of the same type (e.g., PET) in which the spot marker is used during production of a second image. The computer processing system is used to align the two images so that the changes can be seen, for example, using a subtraction procedure, 25 where one image is subtracted from the other.

The processing system(s) 160, 176, 180 may be, or may include, a conventional computer system, such as a personal computer (PC), a server and workstation, a single-board computer, or the like. In one embodiment, the processing 30 system includes a central processing unit, random access memory (RAM), read-only memory (ROM), and a mass storage device, each coupled to a bus system (not shown), as is known in the art. Also coupled to the bus system are a display device (including controller), which may be a 35 cathode ray tube (CRT) 162, liquid crystal display (LCD), or the like; a keyboard 184; a pointing device 186, such as a mouse, trackball, touchpad, or the like; a data

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communication device 194; and a printer 190. The data communication device may be used by the processing system to communicate with the detectors and/or other computer systems or components and may be, for example, a network adapter, a 5 modem, or any other suitable data communication device.

The display device and printer may be used to display and print, respectively, fusion and/or individual images reconstructed by the processing system 180.

It should be noted at this point that some or all 10 aspects of the present invention may be embodied in software. That is, the present invention may be carried out, at least in part, in a computer system, such as processing system, in response to its CPU executing sequences of instructions contained in memory. The instructions may be 15 executed from RAM, ROM, a mass storage device, or a combination thereof. In certain embodiments, hardwired circuitry may be used in place of, or in combination with, software instructions to implement the present invention. Thus, the present invention is not limited to any specific 20 combination of hardware circuitry and software, nor to any particular source of any such software.

It will be appreciated that while reference is made to a single image, multiple images may be obtained for one or both imaging procedures. The images from the second 25 procedure may then be compared with an image from the first procedure (or vice versa) until two images which are superimposable (as indicated by the alignment of the spot marker images) are found. Or, where the computer has capabilities for generating and rotating three dimensional 30 images from the data input, one or both of the three dimensional images from the first and second imaging procedures can be rotated until the spot marker images come into alignment.

The spot marker may also be used to align different 35 images taken in the same imaging procedure, for example, when changes in the body over a short period of time are being observed, such as the progress of a radioactive

isotope through the body. Or the spot marker can be used to align images taken at different depths.

The spot markers of the present invention may also be used in a conventional manner, such as for determining, the 5 locations of features under investigation. For example the position of a cancer tumor may be determined relative to the position of one or more of the fixed points on the spot marker and the information later used in a surgical procedure for excising the tumor. Or, the size of a feature 10 may be estimated by comparing the length of the image with the distance between points on the spot marker image.

It will also be appreciated that the use of the spot marker described herein is not confined to human studies. Animals and inanimate objects may also be studied with the 15 spot marker.

The positron-emitting isotopes and other isotopes used in the embodiments of the spot marker disclosed herein for PET imaging have a longer life than the isotope used for injection into the patient. This allows the sport marker to 20 be reused over a period of months or even years. The radioactive source material used in the detectable substance preferably has a half of at least six months, more preferably, at least one year. Suitable relatively long life isotopes for PET scanning include Na-22 and Ge-68/Ga-68. Of 25 the two, Na-22 may be preferred because of its longer half life. Na-22 has a half life of 2.5 years, giving the radioactive source a usable lifetime of about 4-6 years, Ge-68 has a half life of about nine months, giving the radioactive source a usable lifetime of about 1-1.5 years. 30 Ge-68 is the parent nuclide of Ga-68, which has a half life of about 1 hour. Thus the two nuclides are generally found together in the isotope.

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Having thus described the preferred embodiment, the invention is now claimed to be:

1. A multi-modality spot marker (10, 22, 83, 100, 132) for use as a positioning aid in imaging procedures 5 characterized by:

a body (20, 24, 84, 110, 133);
a plurality of detectable substances (50, 64, 80, 82, 88, 136, 138) supported by the body in fixed relation to each other, a first (64, 82, 136) of the detectable 10 substances being detectable in a first of the imaging procedures and a second (50, 80, 138) of the detectable substances being detectable in a second of the imaging procedures, but not in the first of the imaging procedures.

2. The spot marker of claim 1, further characterized by:

at least one of the imaging procedures being selected from the group consisting of Positron Emission Tomography 5 (PET), Single Photon Emission Tomography (SPECT), Computerized Tomography (CT), and Magnetic Resonance Imaging (MRI).

3. The spot marker of claim 2, further characterized by:

one of the detectable substances (64, 82, 136) being detectable by a PET imaging procedure and including a 5 positron emitting isotope.

4. The spot marker of claim 3, further characterized by:

the positron emitting isotope being selected from the group consisting of Na-22, an isotope containing at least 5 one of Ge-68 and Ga-68, and combinations thereof.

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5. The spot marker of claim 2 or 3, further characterized by:

one of the detectable substances (64, 82, 136) being detectable by a SPECT imaging procedure and including a 5 radioisotope.

6. The spot marker of any one of preceding claims 2-5, further characterized by:

one of the detectable substances (50, 80, 88, 138) being detectable by a CT imaging procedure and including a 5 material of higher density than a subject (143) being imaged.

7. The spot marker of claim 6, further characterized by:

the detectable substance (50, 80, 88, 138) being selected from the group consisting of steel, stainless 5 steel, aluminum, and combinations thereof.

8. The spot marker of any one of preceding claims 2-7, further characterized by:

one of the detectable substances (50, 80, 88, 138) being detectable by a MRI imaging procedure and including a 5 material of higher proton content than a subject (143) being scanned.

9. The spot marker of claim 9, further characterized by:

the material of higher proton content including at least one of a wax and an oil.

10. The spot marker of claim 1, further characterized by:

the detectable substances (50, 64, 80, 82, 88, 136, 138) being selected from the group consisting of radioactive 5 isotopes, materials which are of higher density than a

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subject (143) being imaged, and materials of a higher proton content than the subject being imaged.

11. The spot marker of any one of preceding claims 1-10, further characterized by:

the first detectable substance (64, 82, 136) including a radioisotope having a half life of at least six months.

12. The spot marker of claim 11, further characterized by:

the radioisotope having a half life of at least one year.

13. The spot marker of claim 1, further characterized by:

the body (20, 24, 84, 110, 133) including at least one cavity (56, 70, 72, 74, 76, 78, 92, 120, 126, 134); and

5 at least one of the detectable substances including a radioactive isotope which is held in the cavity by a resin.

14. The spot marker of claim 1, further characterized by:

the first and second detectable substances defining first and second fixed points which are spaced from each 5 other.

15. The spot marker of any one of preceding claims 1-14, further characterized by:

at least one of the detectable substances defining points ($P_1, P_2, P_3, P_4, P_5, P_6, P_7, P_8, P_9, P_{10}$) in three 5 dimensions, allowing alignment in three dimensions of an image produced by the imaging procedure in which the at least one detectable substance is detectable.

16. The spot marker of claim 15, further characterized by:

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the at least one detectable substance defining four fixed points in three dimensions.

17. The spot marker of claim 15, further characterized by:

the body (20) having a pyramidal shape and the four fixed points being defined adjacent corners of the pyramidal 5 shape.

18. The spot marker of claim 1, further characterized by:

the body (133) defining upper and lower surfaces; a cavity (56, 70, 72, 74, 76, 78, 92, 120, 126, 134)

5 extending from one of the upper and lower surfaces;

the first detectable substance being in the form of a pellet received within the cavity; and

the second detectable substance being a radioisotope which is received within the cavity.

19. A spot marker (10, 22, 83) for use as a positioning aid in an imaging procedure characterized by:

a body (20, 24, 84);

at least one detectable substance (50, 64, 88) which is 5 detectable in the imaging procedure, the detectable substance being supported by the body and defining four points (P₁, P₂, P₃, P₅, P₆, P₇, P₈, P₁₀) in fixed relation to each other, allowing alignment in three dimensions of an image produced by the imaging procedure in which the at 10 least one detectable substance is detectable.

20. The spot marker of claim 19, wherein at least one of the detectable substances includes a radioisotope having a half life of at least six months.

21. A method of multi-modality imaging characterized by:

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positioning a spot marker (10, 22, 83, 100, 132) in fixed relation to a subject (143) which is to undergo 5 imaging;

subjecting the subject to a first imaging procedure to produce a first image of the subject, the first imaging procedure generating an image of a first detectable substance carried by the spot marker on the image of the 10 subject;

subjecting the subject to a second imaging procedure to produce a second image of the subject, the second imaging procedure generating an image of a second detectable substance carried by the spot marker on the second image of 15 the subject, but not an image of the first detectable substance;

aligning the images using the images of the first and second detectable substances.

23. The method of claim 22, further characterized by: the spot maker being positioned on an exterior surface (12) of the subject.

24. The method of either one of claims 22 and 23, further characterized by:

at least one of the first and second imaging procedures being selected from the group consisting of Positron 5 Emission Tomography (PET), Single Photon Emission Tomography (SPECT), Computerized Tomography (CT), and Magnetic Resonance Imaging (MRI).

25. The method of any one of preceding claims 22-24, further characterized by:

the first detectable substance including a radioisotope having a half life of at least six months.

26. The method of any one of preceding claims 22-25, further characterized by:

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the second detectable substance including one of the group consisting of materials which are of higher density 5 than the subject being imaged, materials of a higher proton content than the subject being imaged, and combinations thereof.

27. A method of imaging characterized by:

positioning a spot marker (10, 22, 83, 100, 132) in fixed relation to a portion of a subject (143) to undergo imaging, the spot marker including amounts of a detectable 5 substance (50, 64, 88) which define four spaced points (P_1 , P_2 , P_3 , P_4 , P_5 , P_6 , P_7 , P_8 , P_{10}) in three dimensions;

producing a first image of the subject using a first imaging procedure, the first imaging procedure generating an image of the four spaced points defined by the amounts of 10 detectable substance; and

producing a second image of the subject using a second imaging procedure, the second imaging procedure generating an image of the four spaced points defined by the amounts of detectable substance; and

15 aligning the first and second images using the generated images of the four spaced points on the first and second images.

28. A method of forming a spot marker for use in two different imaging procedures characterized by:

supporting an amount of a first detectable substance (64, 82, 136) on a support body (20, 24, 84, 110, 133), the 5 first detectable substance including a radionuclide which is detectable in a first imaging procedure;

supporting an amount of a second (50, 80, 88, 138) detectable substance, which is different from the first detectable substance, on the support body in a fixed 10 position relative to the amount of the first detectable substance, the second detectable substance being detectable in a second imaging procedure.

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29. The method of claim 28, further characterized by: the first detectable substance comprising a radionuclide having a half life of at least six months.

30. The method of claim 28 or claim 29, further characterized by:

the body defining a cavity {20, 24, 84, 110, 133} which holds the first and second detectable substances.

31. The method of claim 30, further characterized by: holding at least the first detectable substance in the cavity with a curable resin.

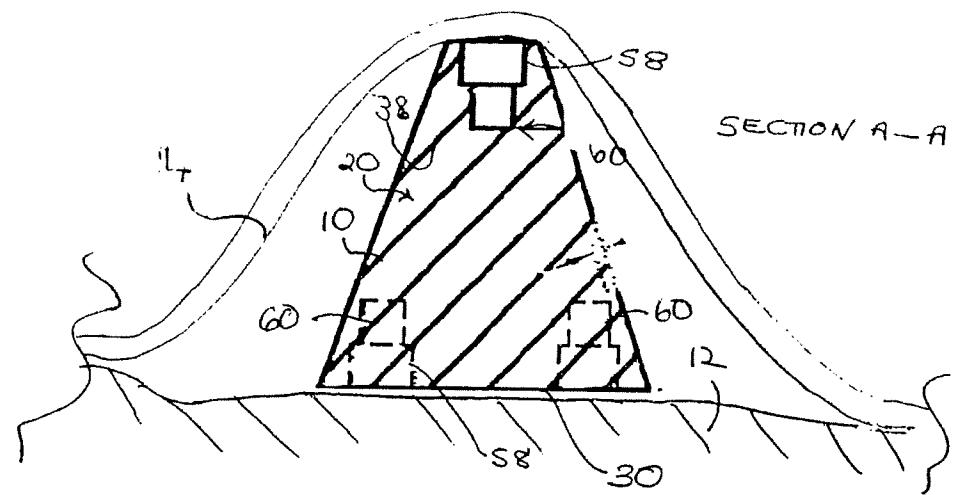


FIG. 1

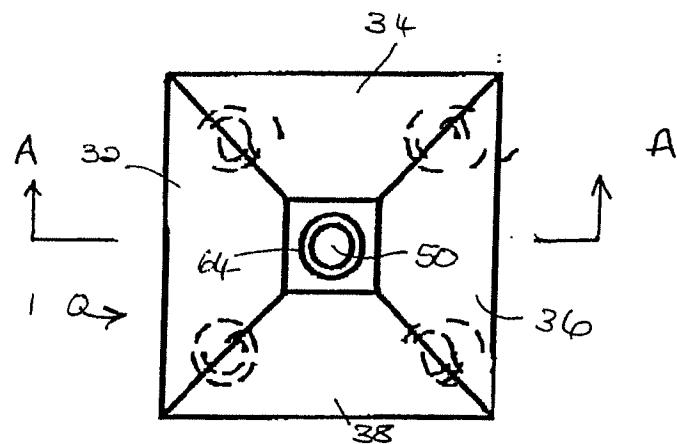


FIG. 2

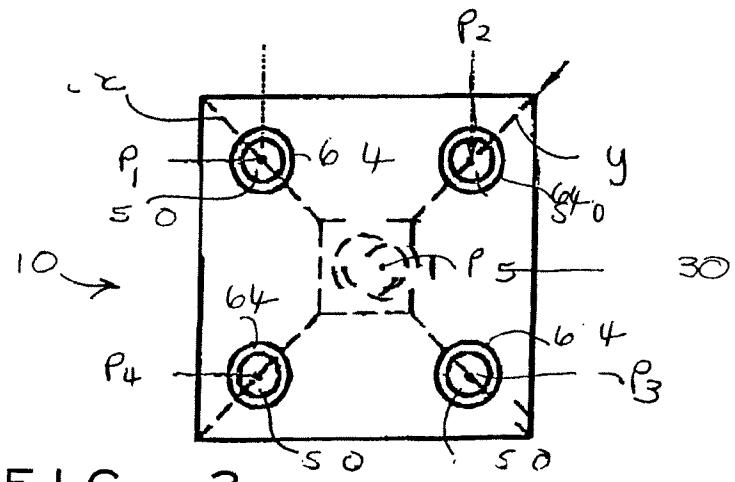


FIG. 3

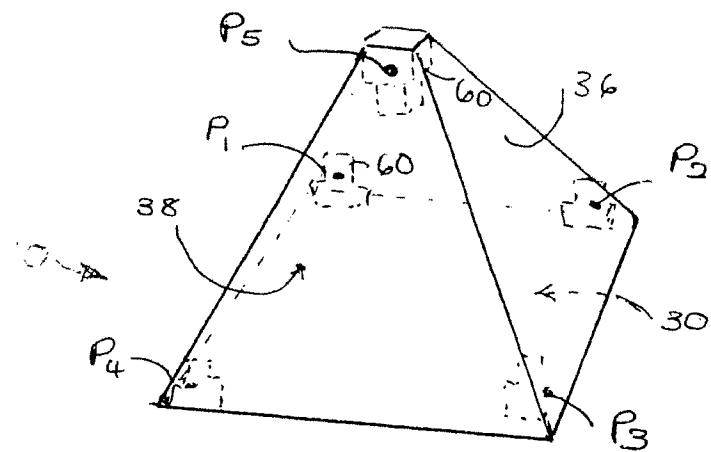


FIG. 4

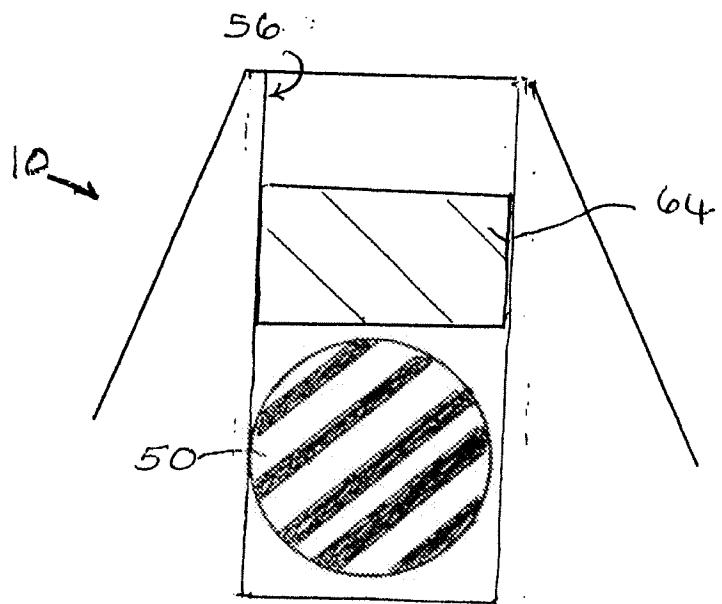
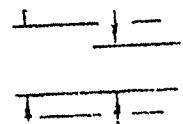


FIG. 5

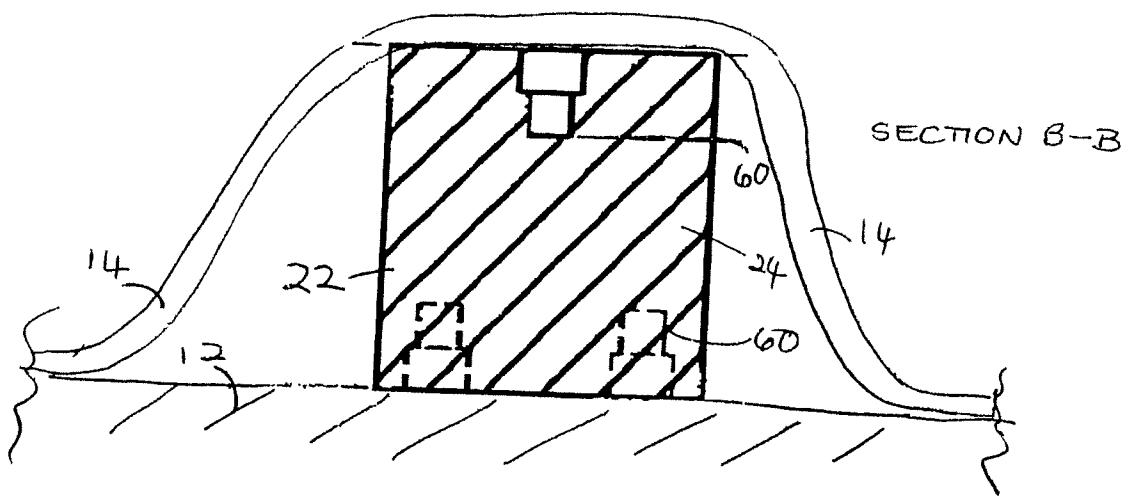


FIG. 6

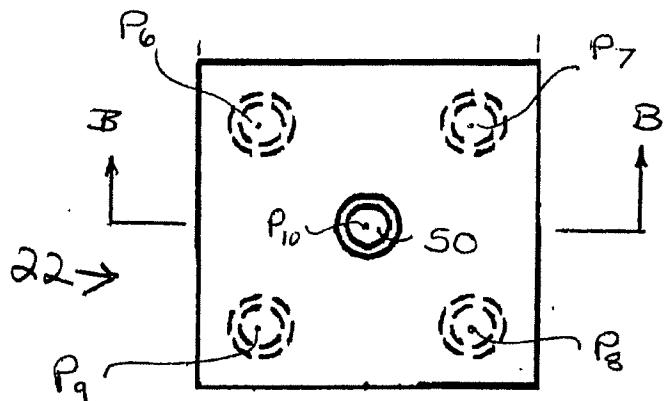


FIG. 7

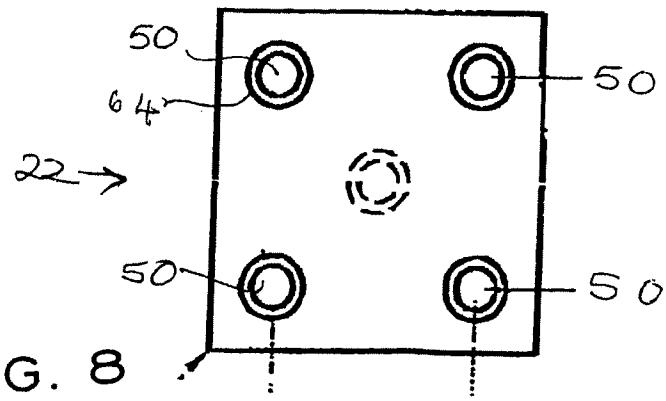
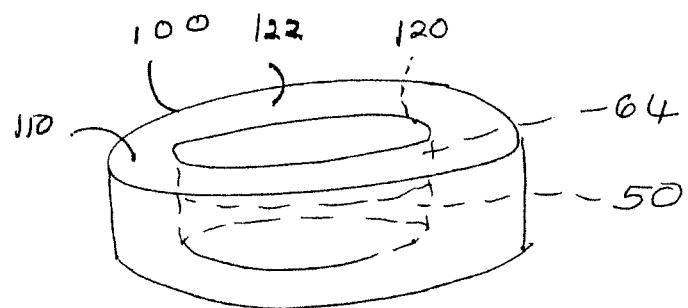
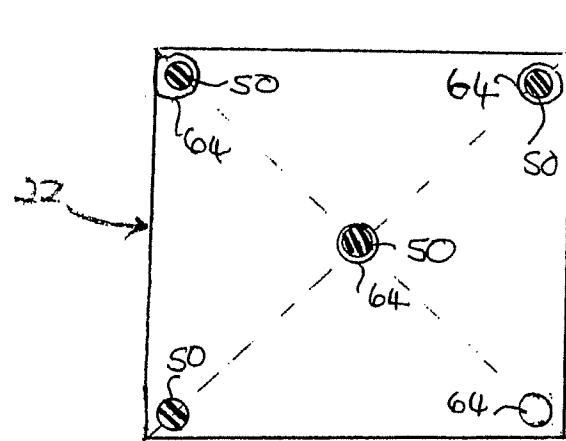
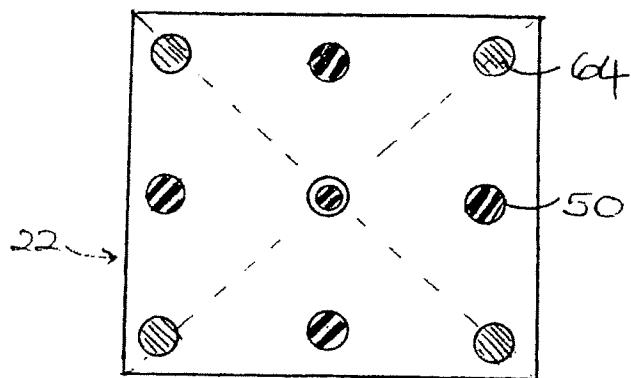


FIG. 8



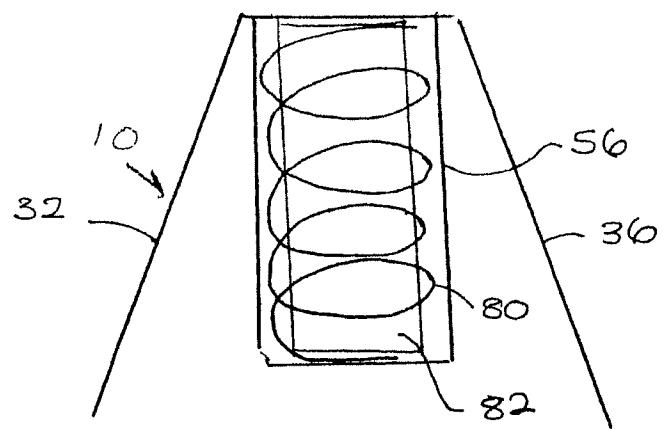


FIG. 11

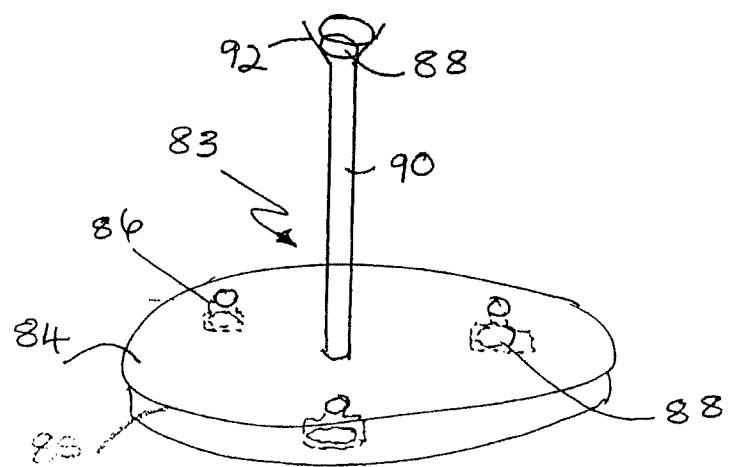


FIG. 12

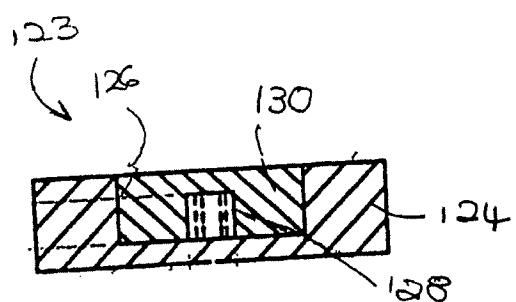


FIG. 14

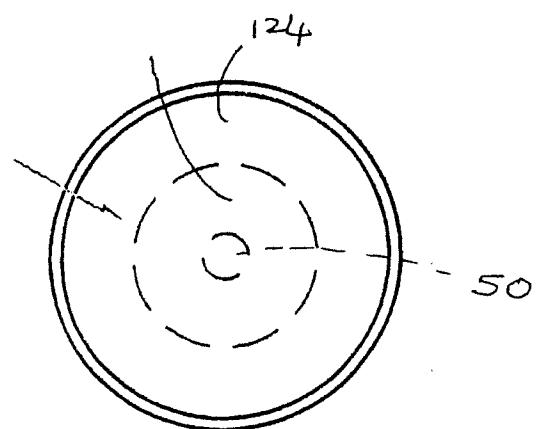


FIG. 15

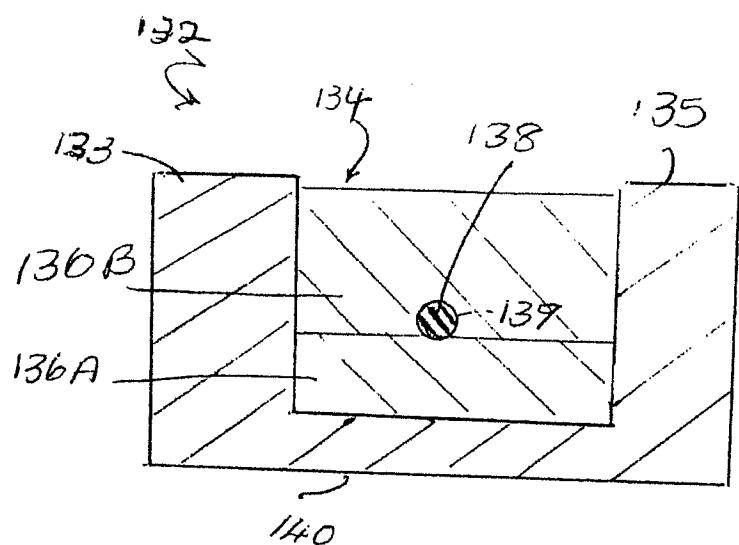


FIG. 16

